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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/755,004	01/05/2001	Anthony P. Shuber	EXT-048	4632

EXAMINER	
CHUNDURU, SURYAPRABHA	

ART UNIT	PAPER NUMBER
1637	

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DATE MAILED: 01/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/755,004	SHUBER, ANTHONY P.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,17-20 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *17* is/are allowed.

6)☒ Claim(s) *1-9,18-20 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Application/Control Number: 09/755,004
Art Unit: 1637

DETAILED ACTION

1. Applicants' response to the office action filed on September 22, 2003 has been entered and considered.

2. The instant application is filed on January 5, 2001, which claims no priority date.

4. Claims 1-9, 17-20, 24 are pending.

Response to arguments

5. Applicants' response to the office action is fully considered and found not persuasive.

6. The following is the rejection made in the previous office action under 35 USC 102(b):

A. Claims 1-6, 8, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Gramley et al. (J Clin. Microbiol., Vol. 37, No.7, pp. 2236-2240, 1999).

With reference to the instant claim 1, 6, 8, 18, Gramley et al. teach a method for detecting a Helicobacter pylori infection wherein Gramley et al. disclose that the method comprises (a) detecting a Helicobacter nucleic acid (DNA) present in a patient stool sample (see page 2236, column 2, paragraphs 1-2, page 2237, column 1, paragraph 1, column 2, paragraph 1, page 2238, column 2, paragraph 1, Fig. 3); (b) identifying a patient having indicative of Helicobacter pylori infection if the amount and length of the nucleic acid (DNA) present in the patient (positive signal intensity) exceeds an amount indicative of an absence (negative signal) of the Helicobacter pylori infection (see page 2238, Fig. 3). Fig. 3 of the disclosure of Gramley et al. indicates southern blot hybridization signals wherein the intensity of signals in comparison to positive signals (presence of H.pylori) and negative signals (absence of H.pylori), indicate the comparison of amount of hybridization signals for the presence or absence of H.pylori infection.

With reference to the instant claims 2-5, Gramley et al. teach that the method comprises (i) detecting a high-integrity (intact) Helicobacter pylori nucleic acid present in a patient sample (gastric biopsy specimens and stool samples) (see page 2238, Fig.2 and 3); (ii) comparing an amount of high-integrity Helicobacter pylori nucleic acid present in the patient sample to an amount of a non-Helicobacter pylori nucleic acid (see page 2238, column 1, paragraphs 1-2, column 2, paragraphs 1-2, Fig. 2 and 3). Fig. 2 and 3 of the disclosure of Gramley et al. indicates universal amplifiable DNA- 224 bp PCR product in case of gastric biopsy specimen (Fig.2) and 148 bp PCR product in case of a stool sample (Fig.3) and southern blot hybridization signals for H.pylori specific amplification products (139 bp). The hybridization signals as compared to the amplifiable (non-H.pylori nucleic acid) in Figs. 2 and 3 clearly indicates the presence or absence of H.pylori infection in comparison to the amount of non-H.pylori nucleic acid.

B. Claims 1-6, 8, 18, 20 are rejected under 35 U.S.C. 102(a) as being anticipated by Powell et al. (WO 00/29618).

With reference to the instant claim 1, 6, 8, 18, Powell et al. teach a method for detecting a Helicobacter pylori infection wherein Powell et al. disclose that the method comprises (a) detecting a Helicobacter nucleic acid (DNA) present in a patient stool sample (see page 8, lines 26-32, page 9, lines 19-25, page 11, lines 1-32, page 12, lines 1-32, page 13, lines 1-2); (b) identifying a patient having indicative of Helicobacter pylori infection if the amount (hybridized product) and length of the nucleic acid (DNA) present in the patient (positive signal intensity) exceeds an amount indicative of an absence (negative signal) of the Helicobacter pylori infection (see page 12, lines 10-21, page 15, lines 20-32, page 17, lines 1-14).

With reference to the instant claims 2-5, Powell et al. teach that the method comprises (i) detecting a high-integrity (intact) Helicobacter pylori nucleic acid present in a patient sample (gastric biopsy specimens and stool samples) (see page 11, lines 1-32, page 12, lines 1-21); (ii) comparing an amount of high-integrity Helicobacter pylori nucleic acid present in the patient sample to an amount of a non-Helicobacter pylori nucleic acid (amplifiable DNA- using universal primers) (see page 11, lines 23-32, page 12, lines 1-8).

With reference to the instant claim 20, Powell et al. also teach that the method comprises determining threshold of H. pylori infection based on the amounts of H. pylori DNA (see page 13, lines 5-12).

Response to arguments:

Applicant's arguments and amendment have been fully considered and are found not persuasive. Applicant argues that Gramley et al. does not teach identifying a patient as having a current infection and refers to the citation on page 2239 of the disclosure of Gramley et al. Applicant further argues that Gramley et al. reported difficulty using PCR to distinguish a current infection from an eradicated one for several weeks after eradication therapy and asserts that Gramley et al. does not teach the method for detecting a current infection and does not teach distinguishing an amount indicative of an absence of current infection. Applicant's arguments have been fully considered and are found not persuasive because Gramley et al. teach that " successful amplification and specific detection of H.pylori DNA directly from stool samples in the majority of infected subjects indicates that this approach is feasible and demonstrates it has a true potential in aiding the diagnosis and management of patients with H.pylori infection", which clearly indicates that the method of Gramley et al. teaches the detection of a patient having H.

pylori infection (current). The amendment reciting the word current is inherent in the teachings of Gramley et al. as stated above.

Similarly, with reference to Powell et al. as noted by Applicant, the reference of Powell et al. is identical in most portions of the disclosure to that of Grimley et al. Applicant's arguments have been considered and found not persuasive. As discussed above Powell et al. also teach that 'successful amplification and detection of H.pylori DNA directly from stool samples demonstrates that such a procedure can be useful for diagnosis and management of patients with H.pylori infection" (see page 16, lines 26-28), indicating that the said procedure can be used to detect current H.pylori infection.

Applicant further argues that neither Gramley et al. nor Powell et al. teach detection of high-integrity H.pylori nucleic acid having about 175 base pairs or more. Applicant's arguments have been considered and found not persuasive because Gramley et al. and Powell et al. teach detection of high-integrity H.pylori infection having 139 base pairs, which meets the claim language of "about" 175 bp. Applicant did not clearly recite the specific length of H.pylori nucleic acid. Therefore, the teachings of Gramley and Powell et al. anticipates the limitations in claim 2. Applicant's arguments regarding claim 18 have been considered and found persuasive. Gramley et al. and Powell et al. teach detection of human nucleic acid (148 bp) in stool samples, the positive control is only with reference to histology analysis. Since the claim 18 does not recite any specific length of human nucleic acid, hence the teachings of Gramley et al. and Powell et al. meets the limitations in claim18.

Thus the disclosures of Gramley et al. and Powell et al. meet the limitations in the instant claims and therefore the rejections are maintained herein.

7. The following is the rejection made in the previous office action under 35 USC 03(a):

Claim 7, 9, 19, and 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gramley et al. (J Clin. Microbiol., Vol. 37, No.7, pp. 2236-2240, 1999) and in view of Lapidus et al. (USPN. 6,143,529).

Gramley et al. teach a method for detecting a Helicobacter pylori infection wherein Gramley et al. disclose that the method comprises (a) detecting a Helicobacter nucleic acid (DNA) present in a patient stool sample (see page 2236, column 2, paragraphs 1-2, page 2237, column 1, paragraph 1, column 2, paragraph 1, page 2238, column 2, paragraph 1, Fig. 3); (b) identifying a patient having indicative of Helicobacter pylori infection if the amount and length of the nucleic acid (DNA) present in the patient (positive signal intensity) exceeds an amount indicative of an absence (negative signal) of the Helicobacter pylori infection (see page 2238, Fig. 3). Fig. 3 of the disclosure of Gramley et al. indicates southern blot hybridization signals wherein the intensity of signals in comparison to positive signals (presence of H.pylori) and negative signals (absence of H.pylori), which indicate the comparison of amount of hybridization signals for the presence or absence of H.pylori infection.

Gramley et al. teach that the method comprises (i) detecting a high-integrity (intact) Helicobacter pylori nucleic acid present in a patient sample (gastric biopsy specimens and stool samples) (see page 2238, Fig.2 and 3); (ii) comparing an amount of high-integrity Helicobacter pylori nucleic acid present in the patient sample to an amount of a non-Helicobacter pylori nucleic acid (see page 2238, column 1, paragraphs 1-2, column 2, paragraphs 1-2, Fig. 2 and 3). Fig. 2 and 3 of the disclosure of Gramley et al. indicates universal amplifiable DNA- 224 bp PCR product in case of gastric biopsy specimen (Fig.2) and 148 bp PCR product in case of a

stool sample (Fig.3) and southern blot hybridization signals for H.pylori specific amplification products (139 bp). The hybridization signals as compared to the amplifiable (non-H.pylori nucleic acid) in Figs. 2 and 3 clearly indicates the presence or absence of H.pylori infection in comparison to the amount of non-H.pylori nucleic acid. However, Gramley et al. did not teach addition of ion chelator (at least 150mM) to the patient sample and immobilized probe hybridization assay.

Lapidus et al. teach a method for improving sensitivity and specificity of obtaining nucleic acids from patient samples wherein Lapidus et al. disclose that the method comprises (i) adding EDTA, an ion chelator to the patient sample, at a concentration preferably at least 150mM (see column 7, lines 28-46); (ii) use of immobilized probe to capture nucleic acid present in a patient sample (see column 10, lines 29-66); (iii) amount of DNA grater than about 200 bp (about includes 150 or 160, or 170 or any number around 200) in length (column 29, lines 42-55); (iv) patient sample comprises bodily excretions (e.g. stool, pus, sputum or saliva) (see column 6, lines 19-23).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of detecting helicobacter pylori nucleic acid as taught by Gramley et al. with the method of adding EDTA as taught by Lapidus et al. because Lapidus et al. states that "use of at least 150mM EDTA greatly improves the yield of nucleic acid from stool sample" (see column 7, lines 40-42). Further, as noted in *In re Aller*, 105 USPQ 233 at 235, More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Routine optimization is not considered inventive and no evidence has been presented that the

concentration of buffer selection performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art. An ordinary practitioner would have been motivated to combine the method of Gramley et al. with the inclusion of limitations (adding EDTA and use of immobilized probe to capture specific nucleic acids) as taught by Lapidus et al. in order to achieve the expected advantage of a rapid and sensitive method for detecting Helicobacter pylori in clinical samples because inclusion of such limitations would enhance the sensitivity and specificity of the method.

Response to Arguments:

Applicant's arguments with respect to the rejection made under 35 U.S.C. 103(a) to claims 7, 9, 19, and 24 have been considered and are found not persuasive. Applicants argue that the combination of the teachings of Gramley et al. in view of Lapidus et al. does not render the instant claims obvious. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992). As discussed above Gramely et al. does teach the limitations in claim 1 and the combination of Gramley et al. in view of Lapidus et al. renders the instant claims obvious because Gramley et al. teach that " successful amplification and specific detection of H.pylori DNA directly from stool samples in the majority of infected subjects indicates that this approach

is feasible and demonstrates it has a true potential in aiding the diagnosis and management of patients with H.pylori infection", which clearly indicates that the method of Gramley et al. teaches the detection of a patient having H. pylori infection (current) and the combination of the teachings of Gramley et al. with the inclusion of limitations (adding EDTA and use of immobilized probe to capture specific nucleic acids) as taught by Lapidus et al. would be obvious to one skilled artisan to enhance the sensitivity and specificity of the method.

Therefore the rejection under U.S.C. 103(a) is maintained herein.

Allowable Subject Matter

8. Claim 17 is allowable.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782 . The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
January 22, 2004

JEFFREY FREDMAN
PRIMARY EXAMINER